# Central corneal thickness measurements in phakic, pseudophakic, and aphakic children with ultrasound pachymetry and different non-contact devices

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# Abstract

**Aims**: Evidence for choosing a satisfactory device for central corneal thickness (CCT) measurement in children particularly pseudophakic and aphakic ones is insufficient. The aim of this study is to compare four differently-measured CCTs obtained using ultrasound pachymetry (UP), Pentacam, partial coherence interferometry (PCI), and specular microscopy (SM) in phakic, pseudophakic, and aphakic children and assess the agreement between the six pairs of the methods.

**Methods**: Children with history of cataract surgery at age six or younger and phakic children were recruited into this study. CCT was measured using UP (Optikon 2000, Rome, Italy), Pentacam (Oculus Inc, Wetzlar, Germany), PCI (IOLMaster 700, Carl Zeiss Meditec AG, Jena, Germany), and SM (Topcon SP-3000P; Topcon Corporation, Japan).

**Results**: One-hundred two eyes (53 phakic, 29 pseudophakic, and 20 aphakic eyes) were included. The mean ages (±SD) of phakic, pseudophakic, and aphakic cases were 9.75 (±3.3), 9.9 (±2.3), and 8.2 (±2.8) years respectively. The mean CCTs (±SE) for phakic children using Pentacam, PCI, UP, and SM were 549.7 (±5.0), 546.5 (±4.5), 565.9 (±5.5), and 506.2 (±4.4) *mm* respectively, for pseudophakic cases were 570.1 (±6.4), 565.0 (±6.1), 571.9 (±6.3), and 524.3 (±6.3) *mm* respectively, and for aphakic participants were 635.3 (±14.2), 635.4 (±14.5), 649.0 (±13.5), and 589.1 (±13.3) *mm* respectively.

**Conclusion**: Compared to Pentacam and PCI, SM underestimated CCT particularly in phakic and pseudophakic children, whereas UP slightly overestimated CCT especially in phakic and aphakic children. Furthermore, Pentacam and PCI had the closest agreement. By contrast, SM had the poorest agreement with the other three methods.


# Introduction

Central corneal thickness (CCT) is an independent parameter for assessing the risk of glaucoma in pediatric population (1). It is particularly important in high-risk children like pseudophakic and aphakic cases (2). Moreover, CCT is an important factor needs to be considered when intra-ocular pressure (IOP) is measured (3). A low CCT underestimates IOP, and a thick cornea with a high CCT overestimates IOP (4). Therefore, we need a measuring device to estimate CCT as accurate and precise as possible, whereas it remains easily applicable, comfortable to use for both children and examiners, and potentially incorporated into a multifunctional device.

There are various contact and non-contact technologies to measure CCT. Ultrasound pachymetry (UP) has been widely used to measure CCT (5) since it is portable and easy to use; however, it is a contact instrument making it uncomfortable for children. The contact probe may pose the risk of corneal epithelial abrasion and infection to the children (6). Furthermore, the indentation pressure as well as the probe misalignment on the corneal surface may make errors in CCT measurements.

Non-contact measuring devices include Pentacam, partial coherence interferometry (PCI), and specular microscopy (SM) among others (5). They are easy to use for examiners and comfortable for children (7). Pentacam measures CCT using the distance between the front and back corneal surfaces. Its CCT measurements in adults have been comparable with those of UP (8). SM has also been used as a non-contact technique, but it frequently underestimates CCT in adults compared to UP (9). PCI has been recently used for CCT measurement, and it could also be an alternative multifunctional technique to measure CCT. PCI-measured CCTs have been comparable with those of UP and Pentacam in adults (8).

However, there is lack of enough evidence to assess the agreement between different CCT-measuring devices in pediatric population particularly pseudophakic and aphakic children (10). That would help pediatric clinicians to choose a satisfactory device for CCT measurement in children. This issue motivated us to make a contribution and measure CCT in phakic, pseudophakic, and aphakic children using UP, Pentacam, PCI, and SM, compare the four measurements within each group of cases, and estimate the agreement between the six pairs of the methods in a pediatric sample in this study.

# Methods

The study was approved by the institutional review board in […] and was conducted in accordance with the Declaration of Helsinki. Informed consent was taken from a parent of each subject.

*Participants*

In this cross-sectional study, we recruited pseudophakic and aphakic patients with a history of combined limbal lensectomy, anterior vitrectomy, with or without posterior chamber intraocular lens (IOL) insertion into the capsular bag at age six or younger. All the IOLs were foldable, hydrophobic, and one-piece, and all the surgeries were performed by one surgeon (M. F.) between 2001 and 2012 in either […]. All the patients underwent cataract surgery at least 5 years before our recruitment to this study. The patients were invited to participate in the study using a phone call from July 2017 to September 2017. Healthy phakic children were recruited from those who came to our clinic for a checkup exam during the same period of time.

*Central corneal thickness measurements*

Before the measurements, all participants underwent a complete ocular examination including slit-lamp biomicroscopy and indirect ophthalmoscopy. Patients with a history of ocular trauma or secondary IOL implantation, central corneal opacity or scarring, corneal edema, microphthalmia, microcornea, or uveitis were excluded from the study.

CCT of each eye was measured using four different methods: PCI (IOLMaster optical biometer 700, Carl Zeiss Meditec AG, Jena, Germany), Pentacam (Oculus Inc, Wetzlar, Germany), SM (Topcon SP-3000P; Topcon Corporation, Tokyo, Japan), and UP (Optikon 2000, Rome, Italy) in a random order other than UP which was always performed last. All the measurements were performed by a single examiner between 8 A.M. and 2 P.M. and on a single day for each participant.

Noncontact pachymetry measurements were conducted as described elsewhere (11). Thereafter, UP was performed last. The child in the supine position was instructed to look straight ahead to a target. The subject's cornea was first anesthetized with one drop of tetracaine (…). The ultrasound probe was then placed as perpendicularly as possible to the center of the corneal surface, and CCT was measured.

*Statistical analysis*

Our data were analyzed using the SPSS Statistics for Windows, version 16.0 (SPSS Inc., Chicago, Ill., USA). Numerical variables are presented as the mean and the standard deviation (SD) or the standard error (SE). The Shapiro-Wilk test was performed to test the normality of the numerical variables. If the data distribution was Gaussian, analysis of variance (ANOVA) was conducted to find differences in numerical variables among the four measurements. Post hoc test with Bonferroni correction was used for the significant results to find any difference for pairwise comparisons. A P-value < 0.05 was considered statistically significant. Scatter as well as Bland–Altman plots were used to assess the agreement between the six pairs of the CCT-measuring methods. The plots were drawn using customized Matlab (Mathworks, Inc.) codes.

# Results

Sixty four phakic (from 35 children), 34 pseudophakic (20 patients), and 33 aphakic (19 patients) eyes were eligible to be included in the study. We were not be able to obtain all the four measurements from 29 eyes because of the subject's fatigue, lack of cooperation, or ocular nystagmus. Therefore, the measurements taken from totally 102 eyes (53 phakic, 29 pseudophakic, and 20 aphakic eyes) were included in our analyses.

The ages of all the participants were within the range of 5 - 18 years. The mean ages (±SD) in phakic, pseudophakic, and aphakic groups were 9.75 (±3.3), 9.9 (±2.3), and 8.2 (±2.8) years respectively.

There were 15 phakic (53.5%) males, 9 pseudophakic (50%), and 8 aphakic (66.6%) males.

The mean CCTs (±SE) for phakic cases using Pentacam, PCI, UP, and SM were 549.7 (±5.0), 546.5 (±4.5), 565.9 (±5.5), and 506.2 (±4.4) *mm* respectively, as shown in Figure 1. There was a significant difference among the measurements within the phakic group (P < 0.001) with the SM being significantly lower than the other three methods (P < 0.001) and the UP being significantly greater than the PCI (P = 0.03). Moreover, the mean CCTs (±SE) for pseudophakic subjects using Pentacam, PCI, UP, and SM were 570.1 (±6.4), 565.0 (±6.1), 571.9 (±6.3), and 524.3 (±6.3) *mm* respectively. The measurements were significantly different (P < 0.001) with the SM being significantly lower than the other three measurements (P < 0.001). In addition, mean Pentacam-, PCI-, UP-, and SM-measured CCTs (±SE) for aphakic cases were 635.3 (±14.2), 635.4 (±14.5), 649.0 (±13.5), and 589.1 (±13.3) *mm* respectively. There was a significant difference among the four measurements (P = 0.02) with the SM being significantly lower than the UP (P = 0.02). Taken together, CCT measurements with SM were lower than those of Pentacam, PCI, and UP particularly in phakic and pseudophakic groups. We will further illustrate it in the next figures.

*Agreement analysis*

The scatter plots for the six pairs of the methods for the 53 phakic, 29 pseudophakic, and 20 aphakic eyes are presented in Figure 2. The dash-dotted lines show the lines of equality for every pair of the methods, and the solid lines represent the correlation between the pairs of the methods. The correlation between each pair of the methods is high where the maximum correlation is between Pentacam and PCI, SM and PCI, and SM and Pentacam. However, the solid regression line has the most proximity to the dash-dotted equality line for the Pentacam-PCI pair.

The agreements between the six pairs of the methods are further illustrated using the Bland-Altman plots in Figure 3. The Bland-Altman plots show the overall mean difference and 95% level of agreement between the pairs of the methods. The maximum agreement is between Pentacam and PCI, followed by Pentacam and UP, and PCI and UP.

Taken Figures 2 and 3 together, Pentacam and PCI are found to have the closest agreement, whereas SM has the poorest agreement with the other three methods. The overall difference between Pentacam- and PCI-measured CCTs is 3.1 *mm*. By contrast, the overall SM-measured CCTs are lower than the Pentacam- and PCI- measured CCTs by 44.7 and 41.6 *mm* respectively. The differences within phakic and pseudophakic groups are greater than that in aphakic cases, as shown in Fig 1.

Furthermore, Fig 3 shows that the overall UP-measured CCTs are slightly greater than the Pentacam- and PCI-measured CCTs by 11.6 and 14.7 *mm* respectively. The differences within phakic and aphakic groups are greater than that in pseudophakic children, as shown in Fig 1.

# Discussion

CCT has been measured using different contact and non-contact devices (12). They include UP, Pentacam, PCI, and SM among others (13). However, it is important to choose a measuring device for pediatric population which is convenient for both children and examiners and as valid and reliable as possible. It is particularly crucial for pseudophakic and aphakic children who are at risk for suffering from glaucoma. A few studies have been conducted to compare different CCT-measuring devices in children (14). In this study, we compared CCT measurements obtained using UP, Pentacam, PCI, and SM within phakic, pseudophakic, and aphakic children.

Our results showed that the overall CCT measurements provided by Pentacam, PCI, and SM were highly correlated, Fig 2. However, Fig 1 showed that SM underestimates CCT compared to Pentacam, PCI, and UP particularly in phakic and pseudophakic cases. Nevertheless, Pentacam- and PCI-measured CCTs were very similar in phakic, pseudophakic, and aphakic children. The Bland-Altman plots in Fig 3 confirmed our findings showing that the closest agreement was between the Pentacam and PCI measurements, whereas SM had the poorest agreement with the other three measuring methods. It is consistent with reports for phakic adults showing that SM-measured CCTs are lower than those obtained using UP (9),

Pentacam (13) or PCI (15). SM in adult studies was found to have a poor agreement with the other CCT-measuring methods since it frequently underestimates CCT (16).

In this study, UP was found to slightly overestimate CCT compared to Pentacam and PCI particularly in phakic and aphakic children, Fig 1. The plots in Fig 3 also showed that UP-measured CCTs were, overall, slightly greater than Pentacam- and PCI-measured CCTs. Our findings are similar to adult reports found a small overestimation of CCT with UP compared to Pentacam (17). However, phakic adult studies showed that there is an acceptable agreement between UP and Pentacam (18-20). In contrast, some adult studies have found that Pentacam-measured CCT is greater than that of UP (8). Further studies may be needed to clarify uncertain results.

The difference among the CCT measurements provided by different devices has been mostly attributed to the different operating principles of the techniques (13); however, the exact cause remains unclear.

It seems that Pentacam and PCI could be appropriate devices for CCT measurement in pediatric population. They are non-contact techniques, comfortable for children, and easy to use for examiners. They could be interchangeably used for phakic, pseudophakic and aphakic children. Their CCT measurements seem to be more accurate than those provided by SM. Therefore, they could be acceptable candidates to serve as substitutes for UP in pediatric population particularly for pseudophakic cases. However, further studies with greater sample sizes are needed to confirm our results.

# Conclusion

In our phakic, pseudophakic, and aphakic pediatric sample, SM underestimated CCT especially in phakic and pseudophakic children compared to UP, Pentacam, and PCI. By contrast, UP slightly overestimated CCT particularly in phakic and aphakic children compared to Pentacam and PCI. Furthermore, Pentacam and PCI had the closest agreement in this study, whereas SM had the poorest agreement with the other three methods. Hopefully, future research will reveal that whether Pentacam and PCI could be interchangeably used for CCT measurement in children, and whether Pentacam and PCI could be satisfactory substitutes for UP in pediatric population.

# Declarations

### Compliance with Ethical Standards

**Conflict of interest:** No conflict of interest has been presented.

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**Author contribution:** *Majid Farvardin:* Funding acquisition, Study design, Data collection and analysis supervision, Manuscript review and edit

*Anis Shamsi:* Data acquisition,

*Amir Norouzpour:* Data analysis, Creation of the software used in the analysis, Data interpretation, Manuscript preparation

*Mohammad-Hasan Jalalpour:* Data acquisition

**Data Availability:** Data will be available upon reasonable requests.

**Animal Research (Ethics):** Not applicable.

**Consent to Participate (Ethics):** Approval was obtained from the ethics committee of Shiraz University of Medical Sciences [No. 10398 and 11958]. The procedures used in this study adhere to the tenets of the Declaration of Helsinki. Informed consent was taken from a parent of each participants.

**Consent to Publish (Ethics):** All the authors approved this version to be published, and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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# Figures

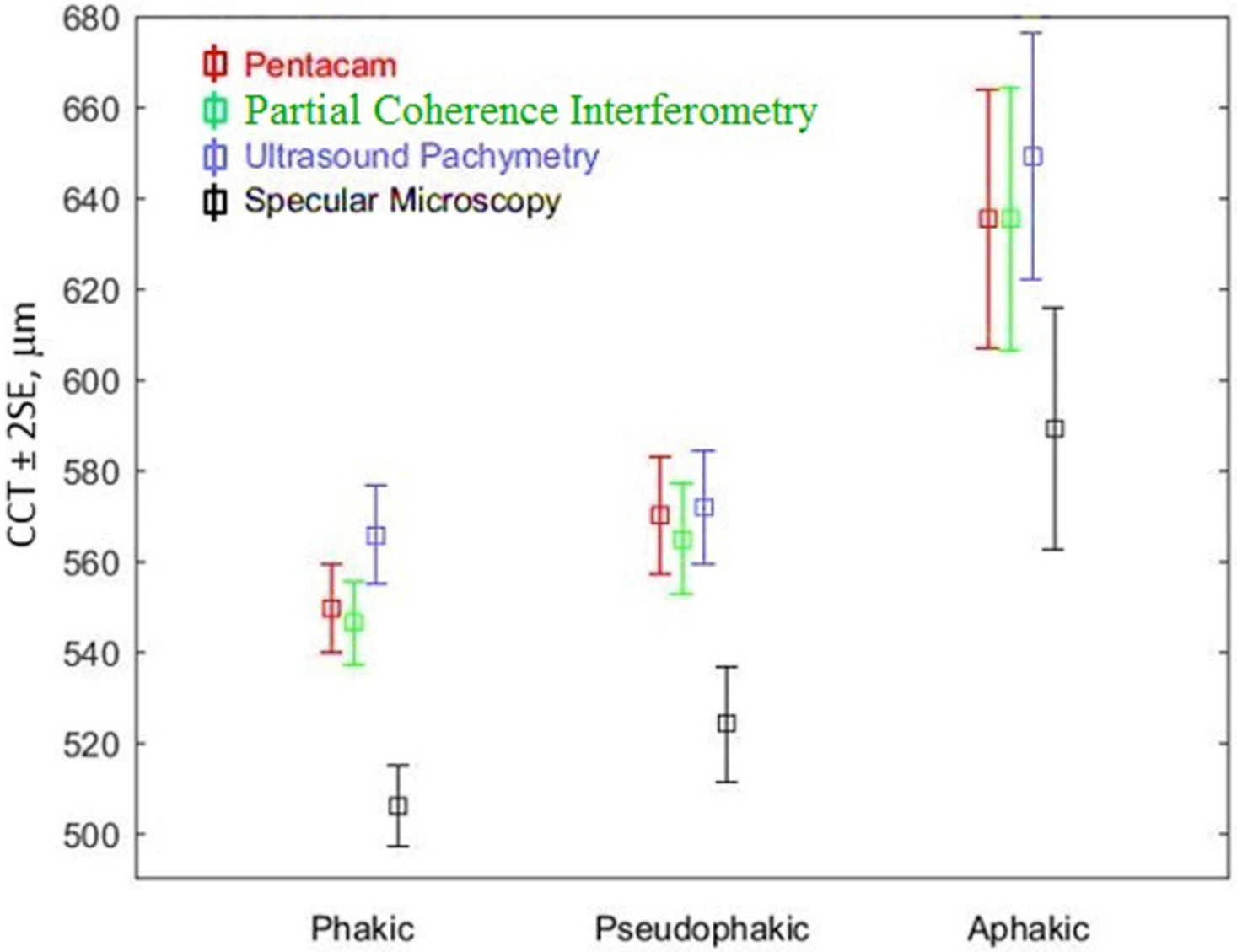
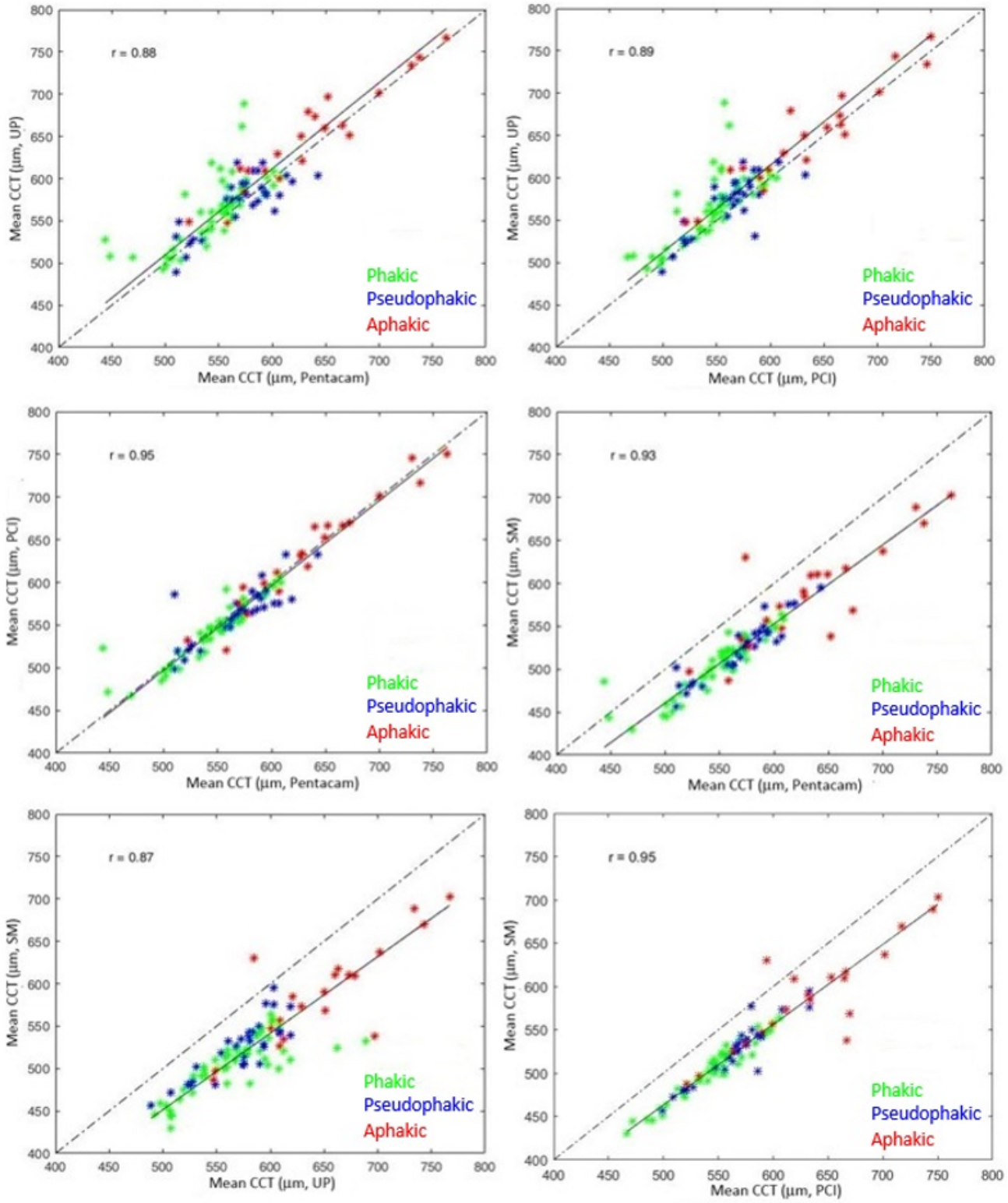


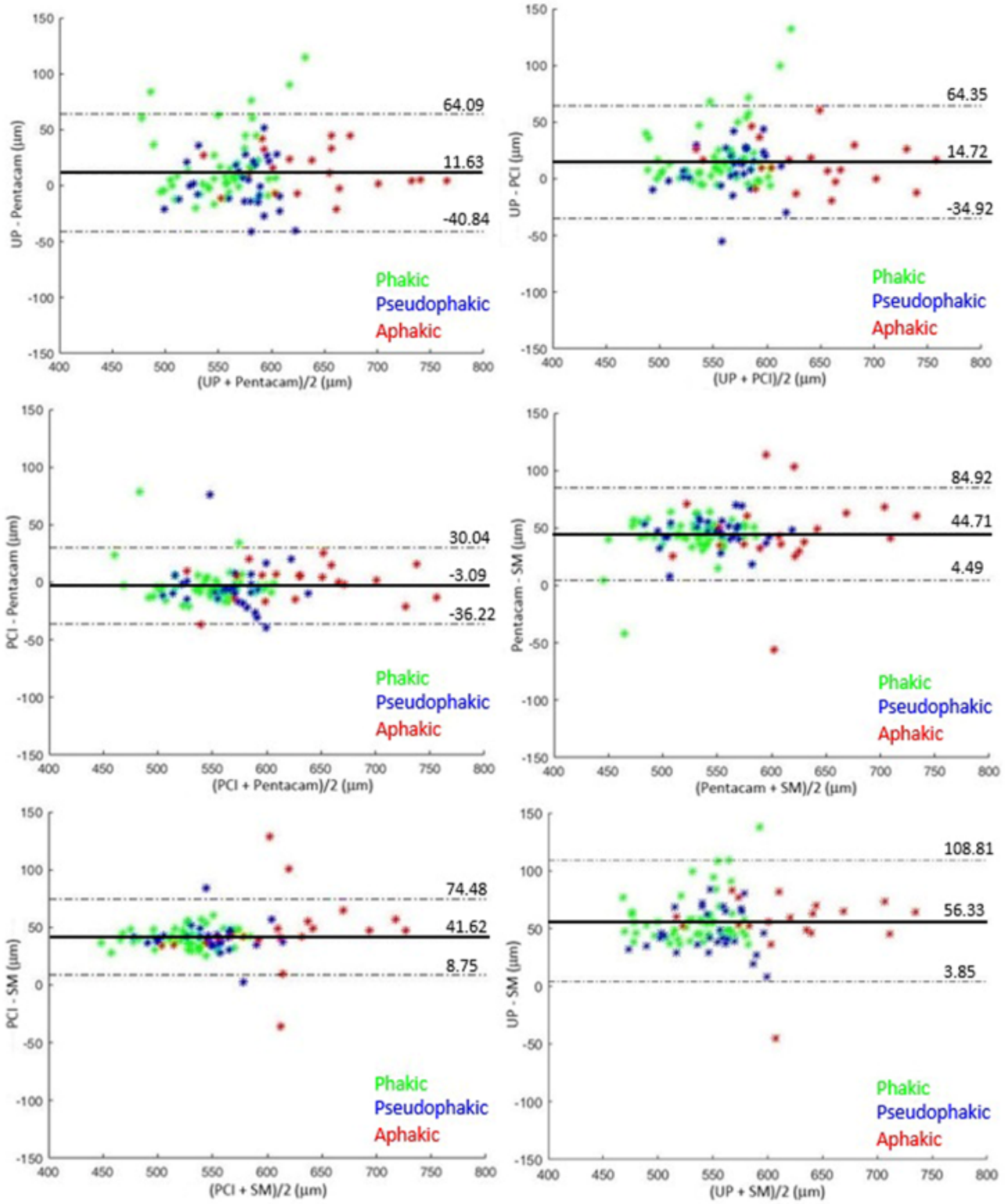

**Figure 1**

The mean CCT for phakic, pseudophakic, and aphakic cases using the four methods. CCT = Central Corneal Thickness, SE = Standard Error.




## Figure 2

Scatter plots for the pairs of the methods. The solid lines show the correlation between the pairs of the methods, and the dash-dotted lines are the lines of equality for the corresponding two methods. The r denotes correlation coefficient. CCT = Central Corneal Thickness, PCI = partial coherence interferometry, UP = Ultrasound Pachymetry, SM = specular microscopy.




## Figure 3

Bland–Altman plots for assessing an agreement between the pairs of the methods. The solid lines correspond to the overall mean difference and the dash-dotted lines correspond to the confidence interval (Mean ± 1.96 SD). PCI = partial coherence interferometry, UP = Ultrasound Pachymetry, SM = specular microscopy.